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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/379,540	08/24/1999	SHLOMO BEN HAIM	BIO-76	1397

7590 10/25/2002

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EXAMINER
GHAFOORIAN, ROZ

ART UNIT	PAPER NUMBER
3763	

DATE MAILED: 10/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/379,540	Applicant(s) HAIM ET AL.	
	Examiner Roz Ghafoorian	Art Unit 3763	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 August 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4-6, 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claim 1 is rejected under the judicially created doctrine of double patenting over claim1 of U. S. Patent No. 6309370 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: an apparatus for inter-cardiac drug administration with a catheter having at least one position sensor which generates signals responsive to an applied field determining position and orientation coordination of the distal end of the catheter by generating signals responsive to the position of the distal end of the catheter within the heart; a drug delivery device which administers a desired dose of a therapeutic drug (i.e. cell) at the site determined responsive to the signals from the position sensor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1, 2, 12-15, 33, 36, 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S Patent 6283951 to Flaherty et al, and further in view of U.S Patent No.6063022 to Ben-Haim.

Flaherty discloses systems and methods that use the cardiovascular system as a conduit to deliver drugs, such as therapeutic drugs, genes, growth factors and the like, directly to selected tissue regions within the body. (Col.1, line 10-15) "Drug" as defined herein includes any therapeutic drugs, genetic materials, growth factors, cells, e.g. myocites, vectors carrying growth factors, and similar therapeutic agents or substances that may be delivered within a patient's body for any therapeutic, diagnostic or other procedure. In one aspect of the present invention, a transvascular catheter system is provided that generally includes a catheter, a drug delivery element, an orientation element, and possibly a puncturing element and/or an imaging element. (Col.3 line 54-62)

When the puncturing element is being oriented, the orientation element is imaged. The imaging element is preferably operated to obtain an image of the orientation element in relation to the surrounding tissue, thereby identifying the ordination of the puncturing

element because of the predetermined relationship between the orientation element and the puncturing element. (Col.5, lines18-25)

Flaherty however, does not teach a position sensor, which generates position and orientation, coordinates or a pressure burst (sensor). Ben-Haim teaches a catheter for cardiac diagnostic and therapeutic system with a position sensor, which generates position and coordinates signals with a pressure sensor.

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to have combine the two teaching, according to Ben-Haim adding the position and pressure sensors allows the caregiver to administer the therapy along the desired path. (Col.4, lines 25-28)

3. Claims 3 --11 rejected under 35 U.S.C. 103(a) as being unpatentable over Flaherty , in view of U.S Patent No.6063022 to Ben-Haim in and further in view of Morocos et al (U.S patent No.5865738).

As noted above, the Flaherty and Ben-Haim disclose a drug delivery device, which consists of a catheter, and delivers cells such as myoblasts or myocyte in to the heart chamber. Flaherty also teaches method of mapping of the interior of the body cavity

Flaherty and Ben-Haim however do not teach a method of assessing the viability of the heart. Morocos discloses a method and apparatus for evaluating the viability of a tissue of interest, particularly that presents as dead but may be merely stunned or hibernating with reduced or no obvious activity, such as contractility (abstract).

This apparatus is carried at the tip of a catheter, which can be guided inside the heart during cardiac catheterization. The new probe allows the physician to: 1) position the probe at a tissue of interest, 2) evaluate the initial state of the tissue, 3) diffuse into the tissue basic ingredients needed for cellular respiration and resulting energy production (oxygen, oxygen-releasing substrates, glucose, low energy phosphates); 4) detect the result of this process by measuring substance uptake, oxygen utilization and/or oxidation reduction (redox) stores of the respiratory enzymes; and 4) optionally detect consequent mechanical activity by ultrasound backscatter technique (in conjunction with a second catheter). (Col.9, line 31) This apparatus allows a one to plan in detail (definition of mapping as found in dictionary was plan in detail) where the damaged tissue was located, and when a myocite or a myoblast should be delivered.

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the these teaching, with the invention of Flaherty and Ben-Haim since according to Morocos cardiologists and cardiac surgeons would both benefit from a procedure which would identify cardiac tissue which has a good probability of returning to normal function. (Col.5, line 60) Faced with the recognition of widened variety of ischemic clinical pictures with variable degree of retained viability, and armed with the knowledge that several conditions previously considered hopeless can now be salvaged if appropriately recognized as viable, cardiologists and cardiac surgeons are increasingly aware of the need to optimize selection form their ever-widening choice of techniques in a way that matches the particular clinical situation. (Col.2 line 10-20)

4. Claims 16-17, 25-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flaherty, in view of U.S Patent No.6063022 to Ben-Haim, and further in view of Gambale et al U.S Patent No.6277082.

As noted above, the Flaherty and Ben-Haim reference disclose a drug delivery device, which consists of a catheter, and delivers cells such as myoblasts or myocyte in to the heart chamber.

Flaherty and Ben-Haim, however, do not teach a catheter which utilizes a laser to create a channel at an oblique angel were the said cells would be delivered. Gambale discloses an invention provides devices and methods for detection of ischemic biological tissue by temporarily altering the temperature of the tissue. (Abstract) Gambale also discloses a detection of an ischemic area of tissue may be followed by a treatment, which may include the implantation of an angiogenic implant alone or in conjunction with a therapeutic agent, such as a growth factor to promote angiogenesis or a cell or gene therapy substance to initiate regeneration of the subject tissue. In such cases, the obturator is adapted to penetrate the tissue in order to facilitate the placement of the angiogenic implant into the tissue alternatively the treatment may comprise creation of channels in the ischemic region by mechanical or laser energy. (Col. 3, line 40-50)

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention as made to have combined the teachings, of Gambale with the invention of Flaherty and Ben-Haim because according to Gambale if the tissue has

remained viable despite the previous deprivation of blood, revascularization, or the restoration of blood flow, to dormant or hibernating tissue can restore the muscle's normal function. (Col.1, line 5-10) Injection of growth factor into myocardial tissue initiates angiogenesis at that site, which is exhibited by a new dense capillary network within the tissue accurate diagnosis and identification of ischemic areas is essential to proper treatment. (Col.2, Line 5-25)

5. Claims 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flaherty, in view of U.S Patent No.6063022 to Ben-Haim, U.S Patent No. 6277082 to Gambale and further in view of German et al U.S Patent No.6258789.

Flaherty, Ben-Haim, and Gamble disclose the claimed invention except teaches the origin of the cell. German discloses cells of a mammalian subject, which are genetically altered to operatively incorporate a gene, which expresses a protein, which has a desired effect. (Abstract). One of the objects of German's method is to produce genetically transformed cells (genetically superior cell), which have incorporated in the their genome exogenous genetic material in the form of a fully functional gene which expresses biologically active and therapeutically useful protein that functions with in the cell. (col.3, line 34-39) any exposure of the DNA of the treated cell to the immune system can result in adverse reaction such as inflammatory reactions to the DNA administered. (Col.2 lines 53-60) Therefore, it would be beneficial to treat these cells with immunosuppressants prior to implantation.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention as made to have combines these teaching, because according to German simply expands on the origins of the cells in Flaherty and Gambale teachings.

7. Claims 34, 37, 40 are under 35 U.S.C. 103(a) as being unpatentable over Flaherty in view of U.S Patent No.6063022 to Ben-Haim, U.S Patent No. 6277082 Gambale, and further in view of Lemelson U.S Patent No.4578061.

Flaherty, Ben-Haim, and Gamble disclose the claimed invention except a catheter with a retractable needle. Lemelson discloses a catheter with a retractable needle and method are provided for injecting a quantity of a liquid. (Abstract) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention as made to have combined these teachings, because according to Lemelson the needle need to be retractable so that it will not penetrate tissue as the device is worked through the body. (Col.1 line 40)

Response to Arguments

1. Applicant's arguments filed 20 August 2002 have been fully considered but they are not persuasive.

a. The applicant has amended claim 1 and has add, "to generate position and orientation coordinates."

Applicant's arguments with respect to claim 1 have been considered but are moot in view of the new ground(s) of rejection.

b. Rejection of Claims 3-11 were traversed the applicant stating 1) Morocco's tissue viability apparatus and method is not at all compatible with the method as described in detail in the Applicant's Specification.2) Morocos et al and the Applicants Calmed inventions are entirely distinct and unrelated 3) the Examiner has used the definition of the word "Mapping" not the definition the applicant has provided in the Specification which states "map identifies areas of the heart muscle that are ischemic as against adequately refused areas on the one hand and infracted non viable areas" page 9, lines 9-10

(1) In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., method of detecting tissue viability) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

(2) Morcos and the Applicant both discuss monitoring tissue viability for the heart for potential treatment of infracted or ischemic heart muscle, therefore they are related art and not distinct from each other.

(3) Morcos teaches a method of identifying evaluating viability of a tissue in the heart, particularly that presents as dead (infarct) vs. ischemic which is the definition used by the application in the specification.

c. Rejections of Claims 16-17 and 25-31 were traversed by applicant stating 1) no position sensor is described by Flaherty 2) Gambale does not address method of delivering a cell wherein the cell is capable of cell fusion with other cells and wherein the cell fusion results in myogenesis. 3) Flaherty does not teach a channel for delivering cells utilizing laser.

(1) Applicant's arguments with respect to position sensor have been considered but are moot in view of the new ground(s) of rejection.

(2) Gambale teaches the implantation of cell or gene therapy substance to initiate regeneration of the subject cell. The word myogenesis means regeneration of muscle cells, and therefore when Gamble teaches regeneration of the subject cell, since he is discussing heart cells it is safe to assume that he could be referring to myogenesis.

(3) Flaherty does not teach the channel for delivering cell utilizing a laser, Gamble teaches the channel and laser, which is why the rejection was made under 35 USC 103, not under 35 USC 102.

d. Rejection of claims 19-24 are traversed by the applicants, the applicant states German does not address treating the cell prior to delivery; utilizing an immunosuppressant; harvesting the cell form the patient, treating the cell prior to delivery; utilizing a genetically superior cell; and utilizing a cell that is a xenograft.

(1) German teaches delivery of cells of a mammalian subject (harvesting) which have been genetically altered (treating with genetic material prior to delivery, genetically superior) to either itself or another mammal (xenograft). It also teaches that introduction of

transforming material via the bloodstream of the individual results in exposure of the DNA and any carrier associated with it to the immune system which leads to adverse affects, therefore to avoid this potentially dangerous side effect one should teat the cells with immunosuppressant.

e. Applicant's arguments with respect to claims 33, 36, 39 have been considered but are moot in view of the new ground(s) of rejection.

f. The applicant traverses rejections of claims 34, 37, and 40, the applicant states that there is no specific teaching in any of the prior at that would lead one of ordinarily skill to combine them.

(1) Claims 34, 37 and 40 teach a retractable needle, the idea of a retractable needle is not unique to the art, and as stated by Lemelson the needle need to be retractable so that it will not penetrate tissue as the device is worked through the body. (Col.1 line 40) that motive is very much related to the inventions of Flaherty and Gambale since both teach a device that needs to enter a cavity in a body.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roz Ghafoorian whose telephone number is 703-305-2336. The examiner can normally be reached on 8:30am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on 703-308-3552. Any inquiry of a general

nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0858.

RG
October 17, 2002

MICHAEL J. HAYES
PRIMARY EXAMINER